American Journal of Pharmacy

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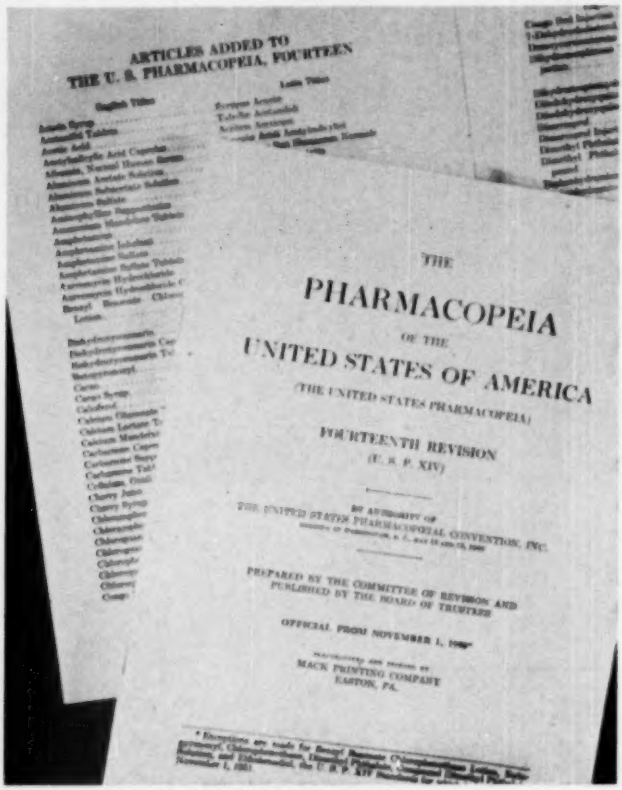

SEE ARTICLE ON THE NEW DRUGS
OF THE U. S. P. XIV

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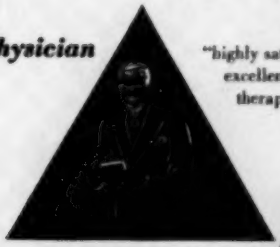

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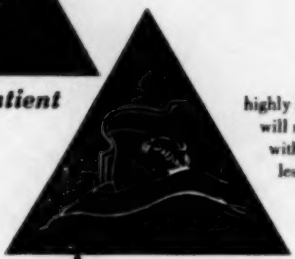

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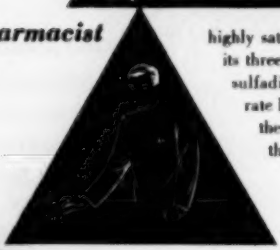

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1. Lobo, D.: Scientific Exhibit, Atlantic City Session, American Medical Association, June 6-10, 1949. *T.M.

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E D I T O R I A L

[Editor's Note.—This month we are featuring a guest editorial prepared specially for this issue by the Director of Pharmacopeial Revision.]

THIS issue and the next of the American Journal of Pharmacy will bring to its readers a resumé of the new features of the fourteenth revision of the U. S. P., which is just now coming off the presses. This revision of the standards for those drugs of stature in modern therapeutics will become official November 1, 1950, slightly less than four years after U. S. P. XIII went into effect. The latter, therefore, has the distinction of being the shortest-lived Pharmacopeia in the entire 130 years of pharmacopeial history. This brief life span reflects first the tremendous pace at which valuable therapeutic agents are being developed nowadays, a fact which led the U. S. P. Convention of 1940 to decree that the Pharmacopeia shall be revised on a five-year basis. Further, it reflects the success of a concerted effort to synchronize the schedule of revision with that of the decennial conventions by completing U. S. P. XIV for distribution prior to the 1950 Convention. Hereafter, it is expected that a revision will appear quinquennially during the years ending in five and zero. This will provide a degree of stability in scheduling not heretofore possible.

The decade of 1940-50 has witnessed a remarkable accomplishment in pharmacopeial revision. To the Revision Committee which has served during this period goes the credit for having prepared three revisions of the Pharmacopeia, the 12th, 13th, and now the 14th. Of course, a valuable legacy was inherited from the out-going Committee, but in view of the great number of new monographs which were made a part of these three books, it is clear that a prodigious amount of work was done. By its nature, this burden could not be distributed uniformly among members of the Revision Committee as the latter was constituted under the by-laws of the 1940 Convention. Therefore, much of the credit for the monumental task now completed is due to a relatively few members of the Committee who were able to devote time almost beyond measure to the task. The difficulty of singling out these individuals is obvious, but the contribution made by Dr. Joseph Rosin, voluntarily and as a work of love, has earned him tribute that is pleasant to record in these pages.

Although written at an unprecedented pace U. S. P. XIV carries many innovations of lasting significance. One of them, which is somewhat revolutionary in character, may escape first notice; it concerns the labeling of vitamins A and D which heretofore has been expressed exclusively in U. S. P. Units. Prior to the isolation of substantial quantities of these vitamins in crystalline form, this practice was necessary and helpful. Now that both of these important food accessory elements can be supplied in crystalline purity, it seems desirable to initiate a movement to express their quantities in absolute units of weight. It may take a generation to complete the changeover; some confusion will be inevitable. However, the long-time advantages are great enough to make it equally inevitable that the change take place. It is fortunate that the advisors to the Revision Committee were farsighted enough to suggest making this step a part of U. S. P. XIV. A similar change has been effected in the case of estrone, the potency of which has been expressed for two decades mainly in terms of biological units. The "Usual Doses" of U. S. P. XIV estrogenic agents are in terms of weight.

Mention should be made of the influence of the ever-present trend to replace biological assays with chemical determinations wherever possible. This has been achieved in the case of estrone, just mentioned, for vitamin A, and the digitalis glycosides, digitoxin and digoxin, all of which are available in a sufficiently pure form to enable their determination by colorimetric assays. That this trend will continue to influence the drafting of the Pharmacopeia is certain. However, U. S. P. XIV still carries several biological assays. An innovation with respect to most of these is a means provided for calculating an approximate standard error. This is a device which enables the assayist to gauge the confidence he can place in the assay result. This distinct advance is based on developments of the last decade which will continue to find application in pharmacopeial revision as long as biological assays must be retained.

U. S. P. XIV is the fifth revision prepared under Dr. E. Fullerton Cook during the three decades of his Chairmanship of the Committee of Revision. While this in itself is a signal and crowning achievement, an even more lasting mark is represented in the incomparably better facilities with which future Revision Committees will be endowed. Through his vision and tireless efforts there has been provided a permanent headquarters for the work of the Committee. Further, the improved organizational structure of the Committee re-

flects his impelling desire for carrying on the revision with the greatest possible efficiency consistent with democratic principles. Those entrusted with the heritage of the past for the purpose of perpetuating this important work face a real challenge. They will be expected to enlarge and extend the influence of the Pharmacopeia in every possible direction. It is not too much to hope that the cooperative spirit which has characterized so many of the efforts of the past will continue and make possible a full realization of every potentiality.

LLOYD C. MILLER

THE NEW DRUGS IN THE U. S. P. XIV

By L. F. Tice *

THE list of articles added to the United States Pharmacopeia, Fourteenth Revision, is more extensive than in any previous revision. A total of 203 new monographs is presented, a number far in excess of the deletions which total only 119.

In a number of cases the new monographs represent simply acceptable dosage forms of basic drugs which themselves were recognized in the U. S. P. XIII. A few new monographs are for drugs and preparations listed in the Eighth Edition of the National Formulary, the Pharmacopeia having exercised its established priority rights in deciding that these were of sufficient importance to warrant inclusion.

The purpose of this article is to discuss briefly the important facts concerning each of these new U. S. P. additions. Since the Pharmacopeia does not list the proprietary names by which many of the official drugs are known, such names will be given so that the pharmacist and the physician may more easily identify certain drugs which under their new official title may be somewhat obscure.

Because of the lengthy list of additions those monographs representing simply new dosage forms of drugs official in the U. S. P. XIII will not be considered. In those cases where the new monograph was formerly in the National Formulary only a brief statement will be made concerning its nature. Long established and well-known drugs will likewise receive only brief treatment.

The drugs considered here are listed according to their index title in the U. S. P.

Acacia Syrup

This product was official in the N. F. VIII. Its formula is unchanged. It has been recognized in the U. S. P. XIV, together with some other similar products, in accordance with the new policy of recognizing suitable vehicles for use by the prescribing physician.

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* Director of the Department of Pharmacy, Philadelphia College of Pharmacy and Science.

Albumin, Normal Human Serum

This is a sterile solution of the serum albumin component of human blood. It is a clear, brownish liquid packaged in a sealed glass container.

The albumin fraction of blood is that fraction largely responsible for the maintenance of the blood's colloid osmotic pressure. This fraction may be used in the treatment of shock and similar emergencies. The use of serum albumin became popular in the Armed Services during the war since the packaged product occupies a much smaller space than an equivalent amount of plasma. The albumin solution is also more stable than liquid plasma, although it is lacking in the other plasma constituents, e.g. fibrinogen and globulins. The usual dose is 25 Gm. which requires 100 cc. of the 25 per cent solution usually furnished. It is, of course, given intravenously, and the dose must be adjusted or repeated in accordance with the needs of the patient.

Aluminum Acetate Solution
Aluminum Subacetate Solution

Both of these products were official in the N. F. VIII. They are useful astringents for external use. The former is somewhat more acid in reaction but the latter tends to precipitate on standing. Both require dilution with water before use, the usual dilution being 9 parts of water to each part of the solution.

Amphetamine

This chemically is racemic α-methyl phenylethylamine. It is a colorless mobile liquid with a characteristic odor. Amphetamine was the first sympathomimetic amine sufficiently volatile to be used in an inhaler for its local effects on the nasal mucosa. It is recognized officially as the component of the next product.

Amphetamine Inhalant

Although official under the title Amphetamine Inhalant, this product is better known as the Amphetamine Inhaler. It consists of Amphetamine, usually aromatized and contained in a suitable inhaler. For many years a product of this type was marketed under the name *Benzedrine Inhaler* by Smith, Kline and French Laboratories, and the product was very widely sold and prescribed for use in relieving nasal congestion. This product was withdrawn from the market in 1949

and replaced with the *Benzedrex Inhaler* which contains a closely related substance, 1-cyclohexyl-2-methylamino propane. This substance possesses much less effect as a stimulant to the central nervous system. The stimulant effect of Amphetamine Inhalers was often objectionable, and the inhalers were being improperly used by some persons for this effect.

Whether Amphetamine Inhalant of the U. S. P. XIV is, or will be, available is not at all certain.

Amphetamine Sulfate

The sulfate of racemic α-methyl phenylethylamine is a white, odorless, crystalline powder. It is recognized officially because of its value as a central nervous stimulant. When given orally it causes marked mental stimulation tending to abolish fatigue and mental depression. It possesses the typical effects of the sympathomimetics, but its effect on the higher nerve centers is so pronounced that it is rarely used except for this specific effect.

Amphetamine Sulfate is used in the treatment of narcolepsy, various types of mental depression, and in certain regimens for the treatment of alcoholism and obesity. The usual dose is 5 mg. A larger dose of 10 mg. may be required, as may several doses a day, depending upon the need of the patient. Care should be exercised in using the drug in patients with coronary involvement or hypertension.

Amphetamine Sulfate Tablets are recognized as a dosage form. They are available in 5 mg. and 10 mg. sizes and are sold as *Benzedrine Sulfate Tablets* by Smith, Kline and French Laboratories.

Aureomycin Hydrochloride
Aureomycin Hydrochloride Capsules

This is the hydrochloride of several antibiotic substances produced by the growth of the organism, *Streptomyces aureofaciens*. It is a yellow, crystalline powder with no odor but a bitter taste.

Aureomycin is one of the newer antibiotics which has given excellent results in the treatment of a number of diseases. It acts as a specific in the rickettsial diseases and possibly some caused by the viruses. It is useful in primary atypical pneumonia, lymphogranuloma venereum, granuloma inguinale, brucellosis, tularemia, pertussis and herpes zoster. The drug is best given orally, although some special technics for its intravenous use have been published. Some gastric distress may occasionally follow its use. Although aluminum

hydroxide gel relieves this gastric distress, its use is open to question since it has been shown to adsorb aureomycin quantitatively. Cottage cheese, given orally, seems to be helpful. The Pharmacopeia recognizes the capsules as a dosage form. These are available as 50 mg. and 250 mg. capsules. The dosage schedule is dependent upon the nature of the infection and its severity, but the usual dose is 500 mg. every six hours.

Benzyl Benzoate Chlorophenothane Lotion

Benzyl Benzoate Lotion was official in the U. S. P. XIII and it is continued in the U. S. P. XIV. This new product contains, in addition to benzyl benzoate, 1 per cent chlorophenothane, commonly known as D. D. T., and 2 per cent ethyl aminobenzoate. The insecticidal action of the chlorophenothane increases the efficiency of the lotion as a scabicide and pediculicide. The ethyl aminobenzoate serves to allay itching. The emulsifying agent in this lotion is Polysorbate 80, commonly known as Tween 80, rather than triethanolamine oleate which is used in Benzyl Benzoate Lotion. *Paracin Liquid* made by Eaton Laboratories and *Topocide* made by Eli Lilly & Co. are products similar to the official Lotion but differing in the emulsifying agent employed.

Bishydroxycoumarin
Bishydroxycoumarin Capsules
Bishydroxycoumarin Tablets

This, chemically, is a 3,3'-methylenebis (4-hydroxycoumarin). It is a white or creamy white crystalline powder with a faint pleasant odor. It is used as an anticoagulant in which capacity it acts by interfering with prothrombin formation in the liver. Unlike heparin it does not produce an immediate effect nor can its proper dosage level be ascertained by the coagulation time. Blood prothrombin must be followed carefully during therapy with Bishydroxycoumarin and, should the prothrombin level drop below 15 per cent of normal, transfusion with fresh whole blood should be instituted and a large dose of Menadione Sodium Bisulfite or some other high potency K-active substance given.

Bishydroxycoumarin is used in selected cases for the prophylaxis and treatment of intravascular clotting. Thus it is used in postoperative thrombophlebitis and pulmonary embolism, in acute occlusion of the peripheral arteries due to emboli or thrombi and in coronary

thrombosis. While it does not possess the immediate action of heparin, it is less expensive and it may be given orally. It is hazardous to employ it without the facilities for the laboratory control needed to follow the level of blood prothrombin.

The administration of Bishydroxycoumarin to patients requires great care. The dosage level for each patient can only be ascertained by laboratory control. The prothrombin level is determined, and then the first dose of 200-300 mg. is given depending upon the size and condition of the patient. On the second day the prothrombin level is determined and a second dose given only if it is above 25 per cent. On successive days a dose is administered only when the prothrombin level is above 25 per cent and the size of the dose regulated accordingly.

Bishydroxycoumarin is sold as *Dicumarol* by a number of pharmaceutical companies. The Pharmacopeia recognizes both capsules and tablets as dosage forms. The usual sizes available are 25 mg., 50 mg., and 100 mg.

Butopyranoxyl

This chemical was originally introduced under the proprietary name, Indalone. It is recognized officially as an ingredient of Compound Dimethyl Phthalate Solution which is used as an insect repellent.

Cacao
Cacao Syrup

These were official in the N. F. VIII. Cacao Syrup is recognized in the Pharmacopeia as a vehicle and Cacao for use in making the syrup. This syrup is commonly known as chocolate syrup or cocoa syrup.

Calciferol

This is essentially pure vitamin D_2. It is made by the irradiation or activation of ergosterol. It is a white, odorless, crystalline substance affected by air and light. It is packaged in sealed containers under nitrogen and protected from light. Each gram contains not less than 40,000,000 U. S. P. units of vitamin D.

Cellulose, Oxidized

This is cellulose in the form of bandage or cotton in which the cellulose has been oxidized with nitrogen dioxide forming cellulosic

acid, the glucose units of cellulose being converted to polyanhydroglycuronic acid units. This causes the cellulose to be so altered that it is somewhat off-white in color and acid to the taste. It is rapidly soluble in sodium hydroxide solution and also slowly absorbed when placed in body tissues. The product is used as a hemostatic agent in surgery acting as an artificial clot, the cellulosic acid having a marked affinity for hemoglobin. Absorption of the oxidized cellulose usually takes place between the second and seventh day but complete absorption may require much longer. Since oxidized cellulose interferes with epithelization it should not be used as a surface dressing and allowed to remain in place. It is also believed to inactivate penicillin but it is doubtful whether this is of clinical significance. It is sold as *Hemopak* by Johnson & Johnson and as *Oxycel* by Parke, Davis & Company.

Cherry Juice
Cherry Syrup

These were official in the N. F. VIII. Cherry Syrup is recognized as a vehicle and the juice as an ingredient to its manufacture.

Chloramphenicol
Chloramphenicol Capsules

This is an antibiotic produced by the growth of *Streptomyces venezuelae* and also produced synthetically. That produced by synthesis has been shown to be identical with the natural substance. It is a relatively simple substance except that it can exist in several isomers, only one of which is recognized. Chemically it is D(-) *threo*-1-*p* nitrophenyl-2-dichloroacetamide 1, 3-propane diol. It is somewhat surprising that it is almost non-toxic in view of the fact that it contains a nitro group attached to a benzene ring.

Chloramphenicol is a white to grayish white or slightly yellow crystalline powder. It is odorless but quite bitter. It is fairly stable in aqueous solution provided the pH is not above 9.5. It is best given orally, but it can be given intravenously dissolved in propylene glycol and water.

Chloramphenicol and Aureomycin Hydrochloride have similar bacterial spectra but in certain diseases one or the other seems more effective. Chloramphenicol is effective in the rickettsial diseases and some of the viral infections. It is useful in brucellosis, pertussis, urinary infections caused by *Ps. aeruginosa*, *E. coli* and *Proteus vulgaris*. It is the drug of first choice in typhoid fever, and it may

also be used in the treatment of gonorrhea, particularly when caused by penicillin resistant organisms. A number of other infections may be controlled by its use.

The drug is usually administered with an initial loading dose of 3-4 Gm. and then 2-3 Gm. are given daily in divided doses. Less severe infections may respond to smaller doses. Chloramphenicol is believed to be almost devoid of toxicity.

The Pharmacopeia recognizes capsules as a dosage form. The drug is available as *Chloromycetin* from Parke, Davis & Company. Each capsule contains 0.25 Gm.

Chlorguanide Hydrochloride
Chlorguanide Hydrochloride Tablets

This, chemically, is 1-(p-chlorophenyl) 5-isopropylbiguanide hydrochloride. It is a colorless crystalline substance or a white powder, stable in air but darkens on exposure to light.

This drug was originally introduced as an antimalarial under the name Paludrine. It is useful for both the prophylaxis and treatment of malaria, acting upon both the erythrocytic and exoerythrocytic forms. The drug appears to act as a causal prophylactic against *P. falciparum* and a partial causal prophylactic against *P. vivax*. Its very low toxicity is one of its outstanding virtues. Recent reports, however, indicate that it may have two important drawbacks. In treating acute malaria it is somewhat slow in controlling the attacks compared with other drugs, and there is some evidence that certain strains of *P. falciparum* acquire resistance to the drug when insufficient amounts are used.

In the treatment of malaria the dose is 100 mg., 3 times a day for 10 days. As a prophylactic 100 mg. is given twice or more times a week.

The Pharmacopeia recognizes tablets as a dosage form and they are available from Abbott Laboratories, Sharp & Dohme and The Upjohn Company. The drug is sold as *Guanatol Hydrochloride* by Eli Lilly & Company. It is also known as *Proquanil, Palusil, Drinupol* and 3359RP.

Chlorophenothane

This chemically is p, p'-dichlorodiphenyltrichloroethane of medicinal grade, a purified form of the well-known D. D. T. It is a white or slightly off-white powder which is slowly affected by light.

It is recognized in the Pharmacopeia only for use in Benzyl Benzoate Chlorophenothane Lotion. It gives to this product even greater scabicidal and pediculicidal action than that possessed by Benzyl Benzoate Lotion.

Only Chlorophenothane intended for use in this official product should be used and not that intended for technical and general insecticidal purposes.

Chloroquine Phosphate
Chloroquine Phosphate Tablets

This chemically is 7-chloro-4-(4-diethylamino-1-methylbutylamino)-quinoline diphosphate. It is a white, crystalline, odorless powder, having a bitter taste. It is discolored slowly on exposure to light.

This substance is an antimalarial which is superior to Quinacrine for the treatment and suppression of malaria. It accomplishes the radical cure of falciparum malaria and acts as an excellent suppressive for vivax. Chloroquine is less toxic than Quinacrine, and it does not stain the skin. There is also a much longer symptom-free time when its use is suspended in vivax malaria. The initial dose for the treatment of malaria is 1 Gm., followed in 6 hours by 0.5 Gm. and then 0.5 Gm. on 2 successive days. As a suppressive the dose is 0.5 Gm. once a week.

The Pharmacopeia recognizes tablets as a dosage form.

It is sold as *Aralen Diphosphate* by Winthrop-Stearns in 0.25 Gm. tablets. It is also known as *Nivaquine-B, Resochin*, SN 7618 and 3377RP.

Congo Red
Congo Red Injection

This is a dark red or reddish brown powder; soluble in water, forming a dark red solution with an alkaline reaction. It is used in the form of the injection in the diagnosis of amyloidosis. Congo red injected intravenously into normal subjects is retained in the blood stream for a considerable time, and no significant quantity appears in the urine. In both type II nephritis and amyloidosis the dye disappears from the blood stream rapidly. In the case of nephritis of type II the dye passes through the kidney into the urine as does albumin. In amyloidosis the dye disappears from the blood, not because it passes through the kidney but because it is absorbed

by the amyloid tissues for which it has great affinity. As much as 60 per cent of the dye may disappear from the blood stream in one hour with none appearing in the urine.

The test itself consists of injecting intravenously 10-15 cc. of a sterile 1.0 per cent solution of Congo Red in normal saline. A 10 cc. blood sample is collected after 5 minutes and 1 hour and a urine sample collected 1 hour and 2 hours after injection. The red color of the dye indicates its presence. The 5 minute plasma sample serves as the standard, and the 1 hour plasma sample is compared with it colorimetrically. Presence of the dye in the urine is readily detected by its color.

The Congo Red test is not infallible, but if it is positive, it may be taken as strongly presumptive evidence of amyloid disease.

7-Dehydrocholesterol, Activated

This substance, also known as vitamin D_3, is a white, odorless, crystalline substance which is affected by air and light. It is made by the irradiation of 7-dehydrocholesterol with ultraviolet light or by activation with cathode rays. This activation results in the opening of ring B of the sterol structure and the formation of a compound having antirachitic activity. The sterol, 7-dehydrocholesterol, is the natural provitamin D of the animal body; when activated it becomes a natural vitamin D as obtained from animal sources. In chicks it is somewhat more active than calciferol (vitamin D_2) in its antirachitic action. Activated 7-dehydrocholesterol has a potency of 40,000,000 International Units per Gm. It must be stored in hermetically sealed containers under nitrogen and in a cool place protected from light.

Dihydrostreptomycin

This is the substance produced by the hydrogenation of streptomycin. The aldehyde group of the streptobiosamine segment of the streptomycin molecule is converted to a primary alcohol group. Dihydrostreptomycin is usually supplied as the hydrochloride or the sulfate. Both occur as white or faintly yellow, granular or powdered substances which are quite soluble in water.

This chemical alteration of the streptomycin molecule has been claimed to reduce its toxicity. Somewhat larger doses of dihydrostreptomycin are given than those of streptomycin itself but its indications are the same. These will be discussed under *Streptomycin* which also has been admitted to the U. S. P. XIV.

Diiodohydroxyquinoline
Diiodohydroxyquinoline Tablets

This, chemically, is 5, 7-diiodo-8-hydroxyquinoline. It is a light yellowish to tan microcrystalline powder which is almost insoluble in water. Diiodohydroxyquinoline is given orally, usually as tablets, in the treatment of intestinal amebiasis and also as a trichomonicide against the *Trichomonas hominis*. The daily dose is 1.5-2.1 Gm. in divided doses, preferably between meals and continued for 20 days. A further course of treatment may be necessary. The very limited solubility of the drug makes intestinal irritation an infrequent reaction.

It is sold as *Diodoquin* by G. D. Searle & Company in the form of 0.21 Gm. tablets.

Dimercaprol
Dimercaprol Injection

This substance was developed during the war as an antidote for Lewisite gas and was called British Anti-Lewisite, a name which was shortened to BAL. Chemically, it is 2, 3-dimercaptopropanol. It has been found to be quite valuable as an antidote for heavy metal poisoning, and it is particularly useful in the treatment of both acute and chronic poisoning due to mercury, arsenic and lead. Dimercaprol also has been recommended to control toxic reactions caused by gold in the chrysotherapy of rheumatoid arthritis. Its action is based upon the formation of a stable 5 membered ring with heavy metal by reason of the affinity between the metal and the sulfhydryl groups of BAL. So great is this affinity that arsenic can be removed from tissue with which it is bound to form the more stable BAL thioarsenite.

It is administered intramuscularly in the form of the Injection. This is a sterile solution in peanut oil made with the aid of benzyl benzoate. The dose is 3-6 mg. per Kg. repeated every 4 hours for the first 2 days. Following this, the dose is administered only twice daily for 8 days or until complete recovery. Some pain may be produced at the site of injection, and excessive doses may cause some toxic reactions.

It is sold as *BAL in Oil* by Hynson, Wescott and Dunning in the form of ampuls each containing 4.5 cc of a 10 per cent solution in peanut oil with 20 per cent benzyl benzoate as a solubilizing agent.

Dimethyl Phthalate
Dimethyl Phthalate Solution, Compound

This is a clear, colorless, oily liquid having a slight aromatic odor. It is insoluble in water but miscible with alcohol, ether and chloroform. Dimethyl Phthalate is recognized as an ingredient of Compound Dimethyl Phthalate Solution which is used as an insect repellent when applied to the skin. This preparation contains 60 per cent Dimethyl Phthalate, 20 per cent Ethohexadiol (Rutger's 612) and 20 per cent Butopyronoxyl (Indalone). Such a combination was found quite effective by the Armed Services during World War II. It is somewhat irritating to mucous membranes, and care must be taken when applying it that it does not get into the eyes.

Diphenhydramine Hydrochloride
Diphenhydramine Hydrochloride Capsules

Chemically, this is β-dimethylaminoethyl benzhydryl ether hydrochloride, and it is the well-known antihistaminic sold by Parke, Davis & Company as *Benadryl*. It is a white, odorless, crystalline powder which slowly darkens on exposure to light. The usual dose is 50 mg. and it is available as both 25 mg. and 50 mg. capsules. The indications for the use of antihistaminics are so well known that no further discussion of this drug seems necessary.

Diphtheria Toxoid and Pertussis Vaccine Combined

This is a sterile mixture of diphtheria toxoid and pertussis vaccine in such proportions that the prescribed dose permits the immunization of a child against both diphtheria and whooping-cough. It is given hypodermically in 3 successive doses at intervals of one month. The product should be stored at a temperature between 2° and 10°, preferably at the lower level.

Epinephrine in Oil Injection

This is a sterile suspension of epinephrine in oil, and it is frequently referred to as "Slow Adrenalin". When given by intramuscular injection it slowly releases the epinephrine, acting as a repository dosage form. Aqueous solutions of epinephrine as the hydrochloride are very transient in their effects. This product is employed in those cases requiring the sympathomimetic effect of epinephrine over a period of time.

It is supplied by Parke, Davis & Company as *Adrenalin in Oil* in the form of 1 cc. ampuls each containing 2 mg. of epinephrine base suspended in peanut oil. A number of other companies supply it under the official title.

Epinephrine Bitartrate
Epinephrine Bitartrate Ophthalmic Ointment
Epinephrine Bitartrate Ophthalmic Solution

Epinephrine Bitartrate is a white, grayish white or light brownish gray, crystalline powder. It is soluble in water and slowly darkens on exposure to air and light. The official ointment contains 1 per cent in a base consisting of hydrophilic petrolatum and 10 per cent water. The official solution contains 2 per cent together with 2 per cent boric acid in distilled water. This solution should be freshly prepared as needed.

Epinephrine Bitartrate is believed to be more stable than the hydrochloride, and its solutions are much less acid in reaction. The official ophthalmic solution has a pH of about 6. Both the solution and ointment are used in the treatment of cataract and to relieve congestion and swelling of the conjunctiva.

Ethohexadiol

This was developed during the war as an insect repellent and was named Rutgers 612. Chemically it is 2-ethylhexane-1, 3 diol. It is a clear, colorless, oily liquid with only a slight odor. Ethohexadiol is an ingredient of Compound Dimethyl Phthalate Solution (see above).

Folic Acid
Folic Acid Capsules
Folic Acid Tablets

Folic acid or pteroyl glutamic acid is now known to be related to substances previously known as "vitamin M", "*L. casei* factor", and "vitamin B_c". It is a yellow or yellowish orange, odorless crystalline powder. Folic acid is insoluble in water and most solvents, but it is dissolved by dilute alkali and hydrochloric or sulfuric acid. Folic acid is of value in the treatment of nutritional macrocytic anemias, including sprue. In pernicious anemia it stimulates erythopoesis, but it does not arrest or reverse the cord damage associated with this condition. It is, therefore, necessary to administer

either liver extract or vitamin B_{12} with folic acid if the latter is given in pernicious anemia. Folic acid also stimulates cell formation in leukopenia. The usual daily dose is 10 mg., and it is available as 15 mg. capsules and tablets. Lederle Laboratories distribute these under the proprietary name of *Folvite*. It is also available under its official title from a number of companies.

Globulin, Antihemophilic

This is a white or nearly white amorphous substance dried from the frozen state. It is a plasma fraction which is capable of shortening the clotting time of hemophilic blood.

It is restored by the addition of sterile, pyrogen-free water or normal saline solution and administered intravenously as a means of arresting hemorrhage in individuals having hemophilia. This condition is hereditary being found only in males but transmitted through the mother. Unless given prophylactic treatment with this globulin, persons with hemophilia may suffer severe hemorrhage and even succumb following a relatively minor injury. The usual dose is 200 mg. which is the contents of one 20 cc. vial. The maximum effect usually lasts for about 12 to 24 hours. This product is available from Cutter Laboratories.

Heparin Sodium
Heparin Sodium Injection

This is a mixture of active principles having the property of prolonging the clotting time of blood. It is usually obtained from the livers or lungs of domesticated mammals used for food by man. Heparin Sodium is a white or pale-colored amorphous, hygroscopic powder. Chemically, heparin is a mucoitin polysulfuric acid ester which is formed in the mast cells of Ehrlich. It acts both as antiprothrombin and antithrombin in the blood stream and prevents coagulation. Heparin Sodium is used in the prophylaxis and treatment of thrombosis, both post-operatively and during transfusion. It has also been used in thrombophlebitis, in frost-bite and gangrene and in the treatment of subacute bacterial endocarditis in combination with massive doses of penicillin. It is usually given by subcutaneous or continuous intravenous injection. Depot forms are also available. The dosage of heparin must be regulated in accordance with the needs of the patient. A coagulation time between 20 and 30 minutes is the usual objective. Intermittent intravenous injection is often used al-

though this does result in considerable variation in the coagulation time. By this route 50 mg. are given every 4 hours. Continuous intravenous injection is given by dissolving 200 mg. of Heparin Sodium in 1 liter of 5 per cent dextrose or physiological sodium chloride solution and administering at the rate of 20-25 drops a minute. It is also given by intermittent intramuscular injection. Depot forms permit the number of injections to be reduced to 1 or 2 every 24 hours. Heparin overdosage may be counteracted by the use of protamine sulfate. Heparin Sodium is supplied as the Injection in several concentrations. The most common strength is 10 mg. per cc. but a high potency product containing 50 mg. per cc. is also available. It is sold by Organon, Inc. under the proprietary name *Liquaemin* and by a number of other manufacturers under its official name.

Homatropine Methylbromide
Homatropine Methylbromide Tablets

Homatropine hydrobromide was official in the U. S. P. XIII and it is continued in the U. S. P. XIV. The methylbromide, a quaternary ammonium derivative of homatropine, was official in the N. F. VIII as were tablets of this drug. These are now recognized by the Pharmacopeia.

Insulin, Globin Zinc, Injection

Globin Zinc Insulin Injection, commonly known as Globin Insulin with Zinc is an almost colorless liquid substantially free from turbidity and insoluble matter.

Globin Zinc Insulin is insulin modified by the addition of globin hydrochloride and zinc chloride. The globin is derived from hemoglobin obtained from beef blood. In the proper ratio and at the proper pH this combination provides a product which is intermediate between insulin and protamine zinc insulin in its onset and duration of action. The period of maximum effect in its hypoglycemic action is between the eighth and sixteenth hour after injection. It is useful in those cases where a single daily injection of regular insulin is not adequate and in cases where protamine zinc insulin is found objectionable. Globin Zinc Insulin seems to produce fewer local reactions than does protamine zinc insulin.

It is administered by deep subcutaneous injection and never given intravenously. Under no circumstances should it be mixed with pro-

tamine zinc insulin nor administered with the same syringe unless the syringe is first thoroughly washed.

Globin Zinc Insulin is packaged in 10 cc. vials containing either 40 or 80 units per cc. It must be stored at a temperature between 0° and 15° but not frozen.

Iodoalphionic Acid
Iodoalphionic Acid Tablets

This substance has the chemical name, β-(4-hydroxy-3,5-diiodophenyl)-α phenyl propionic acid. It is a white, crystalline or a faintly yellow powder having a faint, characteristic odor and taste. It becomes slightly discolored on exposure to light. Iodoalphionic Acid is given orally, in tablet form, for the delineation of the gall bladder in cholecystography. The patient is directed to eat a light, fat-free meal on the afternoon of the day preceding the examination. A dose of 3 Gm. of the drug is taken during or after this meal, and the examination is made the following morning. Iodoalphionic acid is claimed to cause less gastrointestinal distress than tetraiodophenolphthalein, although it sometimes causes nausea, vomiting, headache and other side effects. It should not be given to patients having acute nephritis, uremia or acute gastrointestinal disorders.

Tablets are available containing 0.5 Gm. each, and these are supplied by the Schering Corporation as *Priodax Tablets.*

Iodochlorhydroxyquin
Iodochlorhydroxyquin Powder, Compound

This, chemically, is 5-chloro-7-iodo-8-hydroxyquinoline. It is a spongy, brownish yellow powder with a slight, characteristic odor, and it is affected by light.

Iodochlorhydroxyquin is used internally for intestinal amebiasis, locally as a dusting powder for wounds, skin eruptions etc., and intravaginally in the treatment of *trichomonas vaginalis* vaginitis.

For intestinal amebiasis it is given orally in a dosage of 0.75-1.0 Gm. daily in divided doses for 10 days. A week or a 10 day rest period should be allowed between courses of therapy, and the possibility of iodism should be kept in mind.

The Compound Iodochlorhydroxyquin Powder is used in trichomonas vaginitis. This powder contains 25 per cent iodochlorhydroxyquin, 10 per cent boric acid, 2.5 per cent lactic acid, 20 per cent zinc stearate and 42.5 per cent lactose. It is administered by intravaginal insufflation.

Iodochlorhydroxyquin is supplied by Ciba Pharmaceutical Products, Inc. as *Vioform* and the Compound Powder as *Vioform Insufflate*. The latter is generally used with *Vioform Vaginal Inserts*, which are vaginal suppositories.

Meperidine Hydrochloride
Meperidine Hydrochloride Injection
Meperidine Hydrochloride Tablets

This substance is also known as Isonipecaine Hydrochloride and Pethidine Hydrochloride. Chemically, it is ethyl 1-methyl-4 phenylpiperidine-4-carboxylate hydrochloride. It is a fine, white, crystalline, odorless powder and is quite soluble in water. Meperidine Hydrochloride is a synthetic analgesic which is unrelated chemically to morphine.

The action of meperidine is similar to the combined action of morphine and atropine with the morphine-like action predominant. It differs from morphine in that it is not a potent hypnotic. It is useful for the alleviation of pain, particularly that associated with spasticity. It is often used combined with barbiturates to produce obstetrical amnesia. Although its manufacture, distribution and sale come within the provisions of the Harrison Act, it is claimed to be less addicting than morphine, and its withdrawal symptoms are much less severe.

The usual dose is 0.1 Gm., and it may be given orally or intramuscularly. It is available from Winthrop-Stearns, Inc. as *Demerol Hydrochloride* in the form of the powder, injection and tablets.

Meralluride
Meralluride Injection

This consists of methoxyoxymercuripropylsuccinylurea and theophylline in approximately molecular proportions. The Injection is a sterile solution of Meralluride in water for injection with sufficient sodium hydroxide solution to effect solution. An additional quantity of theophylline may also be added. The Injection is a clear, colorless to faintly yellow liquid, having an alkaline reaction.

It is used as a mercurial diuretic in the treatment of edema associated with cardiorenal disease or nephrosis and acts by reducing the tubular resorption of water. Its use is contraindicated in acute nephritis, kidney disease associated with nitrogen retention, colitis and myocardial infarction.

Since some patients show an idiosyncrasy toward mercurials, the initial dose should be quite small. The Injection usually contains the equivalent of 39 mg. of mercury and 48 mg. of theophylline per cc. The initial dose should not be greater than 0.5 cc. of this solution, given intramuscularly or intravenously. If the patient shows no sign of intolerance to the drug, the dosage is increased to 1-2 cc. given twice weekly.

Meralluride Injection is supplied by Lakeside Laboratories, Inc. in 1 and 2 cc. ampuls as *Solution Mercuhydrin Sodium*.

Mercurophylline
Mercurophylline Tablets

Mercurophylline was official in the U. S. P. XIII as the injection. The U. S. P. XIV has added a monograph on the substance itself and one on tablets. The Injection is also retained. Mercurophylline is the well-known mercurial diuretic sold originally by Campbell Products, Inc. as *Mercupurin* and now sold by this company under the proprietary name *Mercuzanthin*. *Mercuzanthin Solution* corresponds to the official Injection, and it contains 135 mg. per cc. The dose is 1-2 cc. The official Mercurophylline Tablets are available from Campbell Products, Inc. as *Mercuzanthin Tablets*. These are enteric coated so that they may be given orally.

Mercury, Ammoniated, Ophthalmic Ointment

This is an ophthalmic ointment containing 3 per cent of ammoniated mercury in a white petrolatum base, incorporated with 1 per cent liquid petrolatum. Its uses are the same as those of the official Yellow Mercuric Oxide Ointment, but it is more stable.

Mercury Bichloride
Mercury Bichloride Ophthalmic Ointment

Mercury Bichloride is a very old drug. It was formerly official in the U. S. P. and was recognized in the N. F. VIII. Its addition to the U. S. P. XIV was solely as a pharmaceutic necessity for use in preparing Mercury Bichloride Ophthalmic Ointment. This is a 0.03 per cent ointment prepared by dissolving 0.3 Gm. of mercury bichloride in 20 cc. of boiling water and incorporating this with sufficient white petrolatum to make 1000 Gm.

Methamphetamine Hydrochloride

This is the dextrorotary form of the substance commonly called desoxyephedrine. Its official name is Methamphetamine, a name

based upon the fact that it is a homologue of amphetamine. Chemically, it is the hydrochloride of *d*-1-phenyl-2-methylaminopropane. It is a white crystalline powder, soluble in water and alcohol.

Methamphetamine Hydrochloride is quite similar to Amphetamine Sulfate in its pharmacology and therapeutic uses. It is claimed that methamphetamine is somewhat more powerful as a central stimulant but less active in its effect on the cardiovascular system. It is used in the treatment of narcolepsy, depressive mental conditions, postencephalitic parkinsonism and as an adjunct in the treatment of obesity and alcoholism. As in the case of Amphetamine Sulfate, it should not be used in patients having marked hypertension or cardiovascular disease.

Methamphetamine Hydrochloride as compared with Amphetamine Sulfate is at least twice as active, milligram for milligram, since the former is the active *d* isomer and the latter is a racemic mixture. The *l* forms of both drugs are quite weak in their central nervous system stimulant action.

The usual dose for both drugs as given in the Pharmacopeia is 5 mg., but in the same dosage Methamphetamine Hydrochloride would be about twice as active.

Methamphetamine Hydrochloride is available as *d*-desoxyephedrine from a number of sources and under a variety of proprietary names as follows: *Desoxyn Hydrochloride*, Abbott Laboratories; *Desyphed Hydrochloride*, Winthrop-Stearns, Inc.; *Drinalfa*, E. R. Squibb & Sons; *Methedrine Hydrochloride*, Burroughs Wellcome & Co.; *Norodin*, Endo Products, Inc.; *Semoxydrin*, S. E. Massengill Co., and *Syndrox*, McNeil Laboratories.

Methiodal Sodium
Methiodal Sodium Injection

This is sodium monoiodomethanesulfonate. It is a white, crystalline water-soluble powder which is decomposed by light. This is a diagnostic aid used both for intravenous and retrograde pyelography. For intravenous pyelography a quantity of Injection is employed which represents about 2 Gm. of the drug for each 15 pounds (7 Kg.) of body weight. The patient is directed to eat only a soft diet the day before the injection and to take a cleansing enema in the evening. Pyelograms may be made a few minutes after the injection.

In retrograde pyelography a 10-20 per cent sterile solution is used, the lower concentration sufficing for thin patients. Still lower

concentrations may be desirable when stones are suspected. Methiodal Sodium is available as *Skiodan* and the Injection as *Skiodan Sodium Solution* (20 and 40 per cent). Both are supplied by Winthrop-Stearns, Inc.

Naphazoline Hydrochloride
Naphazoline Hydrochloride Solution, Mild
Naphazoline Hydrochloride Solution, Strong

This chemically is 2-(1-naphthylmethyl)-imidiazoline hydrochloride. It is a white crystalline powder which is soluble in water. Its solutions are neutral to litmus and have a bitter taste.

The mild solution contains from 0.045 to 0.050 Gm. of Naphazoline Hydrochloride per 100 cc. and the strong solution contains from 0.093 to 0.107 Gm. per 100 cc. Both solutions are buffered, made isotonic, and they may contain a preservative.

Naphazoline Hydrochloride is a very powerful vasoconstrictor for use in alleviating nasal congestion and swelling. It has a more prolonged action than those drugs related to phenylethylamine, and it is used in lower concentration.

The 0.1 per cent solution is used only for or by adults. Only a few drops should be instilled into each nostril and overdosage avoided. It should not be repeated for several hours. The 0.05 per cent solution is for use in children and on tampons. Since it reacts with aluminum, it should not be used in atomizers made of this metal. Although Naphazoline Hydrochloride is one of the most potent and long-acting vasoconstricting agents, its use, like that of others, over a period of time may cause rebound congestion. Some individuals experience certain side reactions such as central stimulation following its use.

Naphazoline Hydrochloride is sold by Ciba Pharmaceutical Products, Inc. as *Solution of Privine Hydrochloride 0.1%* and *Solution of Privine Hydrochloride 0.05%*.

Nikethamide
Nikethamide Injection

This is N,N-diethyl-3-pyridine carboxamide, an N,N-diethyl derivative of nicotinamide. It is a clear, colorless to yellowish liquid which crystallizes on standing in the cold. It is miscible with water and alcohol.

Nikethamide is used both orally and by injection as a respiratory stimulant and as a stimulant in acute circulatory failure not as-

sociated with cardiac disease. It has also received favorable reports as an antidote in barbiturate poisoning in place of picrotoxin.

The oral dose is 0.5 Gm., but in emergencies the drug must be given intravenously. A 25 per cent weight in volume solution is usually employed for this purpose and the dose carefully regulated. The drug is rapidly inactivated after injection so that for doses exceeding 3 cc. of the 25 per cent w/v solution the administration should be slow and adjusted in accordance with the effects produced in the patient. Excessive doses may produce death from respiratory failure.

Nikethamide is available from numerous sources under its official title, and it is also sold under the proprietary name, *Coramine*, by Ciba Pharmaceuticals, Inc.

Nitrogen

This gas is colorless, odorless and tasteless. It is recognized in the Pharmacopeia for use as an inert gas in the packaging in ampuls of substances sensitive to air or oxygen. Thus, for example, 7-dehydrocholesterol is stored in ampuls under nitrogen.

Para-Aminobenzoic Acid
Para-Aminobenzoic Acid Tablets

Para-aminobenzoic Acid is a white or slightly yellow, odorless crystalline powder which is affected by light. It is administered orally in the prophylaxis and treatment of rickettsial diseases such as Rocky Mountain spotted fever, typhus and scrub typhus.

The oral dose as a prophylactic is 2-4 Gm. in one dose. For treatment the initial dose is 4-6 Gm., followed by 2-3 Gm. every 2 hours. Fluids are restricted in order to raise the blood concentration.

Although official as the free acid it is generally used as the sodium salt.

PABA Sodium, which is the sodium salt of para-aminobenzoic acid, is sold as 0.5 Gm. tablets by Wyeth, Inc. and by Ives-Cameron Co., Inc.

Penicillin Potassium *

This is the potassium salt of an antibiotic substance or substances produced by the growth of *Penicillium notatum* Westling, or of

* No discussion of the clinical uses for penicillin appears since this would entail more space than is available in this review.

Penicillium chrysogenum Thom. It is generally referred to as amorphous penicillin in order to differentiate it from the crystalline variety. The usual daily dose by intramuscular injection is 300,000 units. The usual daily dose orally is 1,500,000 units on a fasting stomach.

Penicillin G Potassium

This is crystalline benzyl penicillin potassium, also known as crystalline penicillin II potassium. It contains not less than 85 per cent of benzyl penicillin potassium. Its properties and uses are the same as the amorphous except that being a crystalline substance it is of more uniform strength, and it is more stable. It is also possible that it produces fewer reactions upon injection.

While amorphous penicillin must be refrigerated even in the dry state, crystalline penicillin is stable up to 3 years without refrigeration. In solution (pH 6.0), crystalline penicillin is stable about 3 days at refrigerator temperatures. Penicillin G Potassium contains not less than 1435 units per milligram. It is given in the same dosage as Penicillin Potassium.

Penicillin G Procaine

This is the procaine salt of the acid of penicillin G. It is a white or faintly yellow crystalline substance or a white, very fine, microcrystalline powder. It is used both orally and by injection with the later route the more frequently employed. It is suspended in either an oleaginous or an aqueous medium for intramuscular injection and given as a repository dosage form.

Penicillin G Sodium

This is crystalline benzyl penicillin sodium differing from the potassium salt only in its strength. It is required to contain not less than 1500 units per milligram, a figure slightly higher than that for the potassium salt. This difference is only because of the lower atomic weight of sodium as compared with potassium. This results in the sodium salt having a lower molecular weight than the potassium salt and a higher potency mg. for mg.

Penicillin, Buffered Crystalline

This is either crystalline potassium penicillin or crystalline sodium penicillin, buffered with 4-5 per cent of sodium citrate. It is intended for oral use. The sodium citrate is to minimize the destructive influence of gastric acidity on penicillin.

Penicillin for Inhalation

This material is crystalline penicillin potassium, crystalline penicillin sodium or penicillin procaine with or without suitable harmless diluents. Penicillin in the form of a very fine powder is administered by inhalation into the nose and upper respiratory tract to combat infections in this region. Penicillin is also administered in solution formed by dissolving soluble tablets in a small porton of water and atomizing the solution into the respiratory tract. A number of commercial devices are available for penicillin administration by this route such as the *Aerohaler* or *Manolator* sold by Abbott Laboratories, the *Penlator* sold by Lederle Laboratories, the *Penaire Inhalator* sold by Sharp & Dohme Inc., and the *Penicillin Dispolator* sold by E. R. Squibb and Sons. Several other companies sell special Inhalers for administering penicillin by inhalation.

Penicillin Procaine for Aqueous Injection

This substance is a sterile, dry mixture of penicillin procaine and one or more suitable, harmless suspending or dispersing agents with or without a buffer. Such products are prepared for injection by the addition of the prescribed amount of water for injection and agitation until the material is in thorough suspension. It is then withdrawn with a sterile syringe and injected intramuscularly. Before the injection is made the plunger should be withdrawn slightly to be certain that the needle has not penetrated a vein. The usual dose of penicillin procaine is 300,000 units a day but larger doses are often administered. When injected intramuscularly, this product forms a depot in the tissue from which the penicillin is slowly released. A single injection provides therapeutic blood levels for at least 24 hours.

Penicillin Procaine for Aqueous Injection is sold under the official name by a number of companies and as:

Aquacillin by Schenley Laboratories
Crysticillin by E. R. Squibb & Sons
Diurnal Penicillin by the Upjohn Co.
Duracillin Aqueous by Eli Lilly & Co.
Sharcillin by Sharp & Dohme, Inc. and
Wycillin Improved by Wyeth, Inc.

Penicillin Procaine in Oil Injection

This is a sterile suspension of penicillin procaine in oil, with or without the addition of suitable and harmless hardening agents. The oil generally employed is peanut or sesame oil and most products in this category contain 2 per cent aluminum monostearate. This latter substance forms a thixotropic gel with the oil, helping to keep the penicillin procaine in suspension. It may also help retard the absorption of the penicillin from the site of injection.

As a depot form of penicillin this product has completely displaced the U. S. P. XIII product Penicillin in Oil and Wax. Some physicians favor Penicillin Procaine for Aqueous Injection, but there are advantages and disadvantages with each type of product, the oil suspension as well as the aqueous. The dose, injection site and precautions are the same for both products. A number of companies sell this product under the name Procaine Penicillin in Oil with Aluminum Monostearate. It is also sold as:

Depo-Penicillin by The Upjohn Co.
Flocillin 96 by Bristol Laboratories
Hypercillin by Cutter Laboratories
Lentopen by Wyeth, Inc.
Millicillin by E. S. Miller Laboratories, Inc.
Monocillin by Schenley Laboratories
Pazillin by Sharp & Dohme, Inc.
Parencillin by The Wm. S. Merrell Co.
Neocillin by Walker Vitamin Products and
4 Day Hypercillin by Cutter Laboratories

(To be continued.)

SELECTED ABSTRACTS

Anticoagulant Therapy. H. W. Fullerton and G. Anastasopoulos. *Brit. Med. J.* No. 4643:1492 (1949). The use of heparin and dicoumarol in the prophylaxis and treatment of thrombosis has been established. Dicoumarol is usually used over a prolonged period of time while heparin is more frequently used over a short period. The dosage of these drugs varies considerably with the individual patients, but the control of the dosage is most important for a hemorrhagic tendency may severely complicate treatment. Dicoumarol is given orally and is thought to act by lowering the prothrombin and, thus, the coagulability of the blood.

The control of dosage being so important, the techniques used for estimating the prothrombin levels are likewise important. However, the different techniques for estimating prothrombin levels have not been thoroughly understood, and much confusion has arisen from their use. The authors have studied the use of these techniques with resulting contribution to our knowledge of them.

The simplest theory of blood coagulation can be summed up in two steps: (1) thrombokinase + prothrombin + calcium → thrombin; (2) thrombin + fibrinogen → fibrin. The main source of thrombokinase is thought to be a precursor in the plasma. Quick's method of prothrombin estimation is based upon this theory. The steps in the test are: (1) 4.5 cc. of blood is mixed with 0.5 cc. of oxalate solution which removes the calcium and thus prevents the first step in coagulation. (2) To 0.1 cc. of plasma 0.1 cc. of rabbit brain powder suspension (a source of thrombokinase) is added and the mixture incubated. (3) Then 0.1 cc. of calcium solution is added and the time between this addition and the formation of fibrin is considered as the prothrombin time (or accelerated clotting time). The amount of calcium and thrombokinase being controlled, the only variable in step 1 is the amount of prothrombin, thus the test is an estimation of the amount of prothrombin. The smaller the amount of prothrombin the longer the time before enough thrombin is formed to bring about stage 2. The brain powder varies in potency, and thus considerable variation has been found with this test. Russell viper venom was suggested as a source of thrombokinase. Experiments had shown the viper venom to have powerful thrombokinase action showing little variation in potency. A third variation in the test technique was a combination of ovo-lecithin and venom. The

normal prothrombin times found with these 3 techniques was 15 to 30 seconds, 18 to 25 seconds, and 6 to 10 seconds, respectively.

This potentiation of the action of venom by ovo-lecithin led to experiments and reasoning which concluded that a lipoid substance is essential for the coagulation of blood. It had been shown that fat-free plasma would not coagulate upon the addition of fat-free thrombokinase and calcium. It was felt that the concentration of lipoid factor in the blood probably varies sufficiently to alter the coagulability of the blood. If this lipoid factor is necessary for coagulation, the various test agents used in the experiment will give different results. When venom plus lecithin is used and optimum amounts of thrombokinase and lipoid factor are added, the test measures variations in the prothrombin level. Tests indicated that the brain powder contained variable and suboptimal amounts of thrombokinase but that this method essentially measured prothrombin and not changes in coagulability due to variations of the lipoid factor. When venom alone is used, we have a thrombokinase which is fat-free and thus acts as a test for the variations in the concentration of the lipoid factor in the blood so long as the prothrombin level is constant.

Thus, when the dosage of dicoumarol is controlled by tests using venom plus lecithin, an evaluation is obtained of the reduction in prothrombin produced by the treatment. However, this reduction in prothrombin does not accurately represent the effect of dicoumarol on the coagulability of the blood for experiments involving the effects of alimentary lipaemia revealed that when the prothrombin level was depressed by dicoumarol a compensatory increase in the lipoid factor occurred. The test using venom alone reflects this alteration in coagulability but does not accurately determine the reduction in prothrombin. One other factor of great importance was that slight hemolysis causes considerable shortening of the prothrombin time when the venom test is used but not when the venom plus lecithin is used.

The authors suggest the use of both venom and venom plus lecithin tests in the control of dicoumarol dosage, maintaining the clotting times at 35 to 40 seconds and 25 seconds respectively. Thus, there is less prolongation, proportionately, with the venom test, for larger doses of dicoumarol are required to produce the same prolongation of clotting time by the venom test as with the venom plus lecithin test.

Six Year Follow Up of the Treatment of Early Syphilis With Penicillin. J. F. Mahoney, R. C. Arnold and A. Harris. *J. Venereal Dis. Inform. 30*:350 (1949). The rapid response to penicillin therapy of early syphilis showed great promise, but it is only after prolonged follow-up periods that the real value of this rapid treatment can be evaluated. The four patients described in this report were observed in a satisfactory manner for a post treatment period of about 6 years.

Each young male patient was originally diagnosed by positive darkfield examinations of primary characteristic lesions. The duration of the lesion did not exceed 10 days in any of the patients when first observed, hence, the serologic tests were inconclusive. However, by the end of the period of therapy each patient was well into the seropositive phase. There was no history of previous syphilis in any of the patients. Treatment consisted of the intramuscular administration of 25,000 units of amorphous penicillin at 4 hour intervals for a total of 48 injections. The only patient to receive additional treatment was one of the 4 who was reinfected as evidenced by a darkfield positive lesion in conjunction with gonorrheal urethritis about 300 days after the original treatment. Re-treatment consisted of 40,000 units of penicillin every 3 hours for 60 injections.

In the follow-up of the patients, physical examinations were given at intervals, but most reliance was placed upon serological tests. It was felt that in the event of relapse serological evidence would precede or at least accompany any clinical evidence. The serological tests employed were the Kline exclusion precipitation and diagnostic precipitation, Mazzini flocculation, Kahn precipitation, Hinton flocculation, Eagle flocculation, and the Kolmer simplified complement-fixation qualitative tests. The Mazzini flocculation and Kahn precipitation quantitative tests were also employed during the first few months following treatment. Spinal fluid examinations indicated no evidence of abnormal changes. In all 4 of these patients observed for about 6 years the serological tests had remained negative for over 3 years, and the men were clinically well. Thus in this small series the long range use of penicillin in the treatment of early syphilis has been vindicated.

BOOK REVIEWS

Pharmaceutical Selling and Detailing. By Arthur F. Peterson. McGraw-Hill Book Co., New York, 1949, $4.50.

Anyone who is acquainted with Mr. Peterson's work in the drug trade will recognize that this book is a distillation of his own extensive and varied experience. People with such views would include just about everybody who has had a responsible position for any length of time in marketing prescription products. For many years Mr. Peterson has been a faithful and alert observer and participant in drug trade conferences and meetings throughout the United States. He also has talked over its problems individually with many different members of the drug trade. This personal acquaintance extends from its top leaders to students and apprentices newly entered in the field.

It is evident from the book that the author has the ability to put down the results of these observations and experiences in a manner that is logical, well organized and systematic. The book is, in fact, a review and analysis of pharmaceutical selling and detailing as the author has experienced it. All too few people can describe and look into their professional careers in such a way that the reader is informed and, in fact, inspired. Mr. Peterson has steered a careful course. He has avoided making his book a lackadaisical series of loosely connected anecdotes. Likewise he has stayed away from the pedestrian prose and tortured style of the author inept in writing craftsmanship who "takes his pen in hand."

His book is a human document written in a style that befits the dignity and importance of the subject. It is a book which a sales executive can assign with confidence as required reading by those whose work he supervises. Indeed, sales executives in the drug trade can read this book themselves with interest and profit. It will help to organize and orient day to day practices that have been used so long that they are now carried out with little or no conscious thought. In addition, this is a book that drug store proprietors can read enjoyably. It will help them to understand the motives that lie behind the visits of manufacturers' representatives to them and nearby physicians. More important, it may inspire these members of the retail trade to detail the physicians and other professional

people in the vicinity of their stores in the same manner and for the same reasons as do the manufacturers' representatives.

As a human document the book is necessarily incomplete and controversial. For it to be otherwise would destroy the fine flavor of personal opinion which to this reviewer gives the book its outstanding individuality. In the discussion of "fair profit, fair dealing and fair trade" in Chapter II, the author speaks out boldly against inside prices secretly given to favored retailers and other customers. With such a stand, there can be no quarrel. The application of the same designation of "chiseler" to other forms of price cutting is not necessarily proper or fair. One of the surest ways to fall behind is to fail to keep one's prices competitive.

If it had been my responsibility to write instead of to review a book on this subject, I would have railed against the deals, propositions, allowances and other complications that make the price lists of some prescription product makers as intricate and hard to understand as the rate schedule of a metropolitan electric light company. I probably would have put in more about the services of wholesale druggists in the marketing of prescription products and the advantages and disadvantages of selling direct to retailers. I am sure I would have included some observations on the fundamental inconsistency in the competitive enterprise system of this country, of drug store proprietors and other members of the drug trade seriously proposing legal restrictions to end or reduce "needless duplications" in prescription products.

On the other hand, Mr. Peterson's book has whole sections and chapters on subjects that I know I would not have had neither the wit to include nor the necessary knowledge and experience to write about if I did know of their existence. Therefore, I have enjoyed and profited by reading Mr. Peterson's book.

PAUL C. OLSEN

Die Ausbildung des Drogisten, Band 1. Drogistenpraxis von Franz Berger, Wien. 351 pages with 258 illustrations, 1949 Publisher: Wilhelm Maudrich, Vienna. $6.30.

To those who have occasion to use information concerning the practice of the "Drogist" in European countries this book will be useful. It must be stated, however, that there is no analogous pro-

fession practiced in the United States. A "Drogist" is not academically educated, he handles crude drugs and chemicals and to a certain extent pharmaceutical preparations as well, but mostly for use in veterinary practice. Never is he permitted to sell any compounded preparations or proprietaries intended for human therapy. The schools where a "Drogist" obtains his training are more or less trade schools. Chemistry, physics and pharmacognosy are taught as well as the manufacture of certain preparations most frequently sold by the "Drogist."

This book then, which is volume I of a series, *The Training of the "Drogist"*, deals in its first section with the physical aspects of the laboratory, handling of equipment and apparatus, and certain basic technical operations. This section is intended for the retail "Drogist", but in the second section the author turns to problems and methods of preparation encountered in large scale manufacturing, i.e. in industry. This section also attempts to make a "Drogist" more familiar with some of the official processes, since some "Drogisten" are employed by pharmacists in their laboratories.

A very large chapter is devoted to the discussion of cosmetic preparations, and this part of the book supplies particularly useful information for the pharmacist. This section is subdivided into 20 chapters such as: The skin and its care, a discussion of the anatomy and physiology of the skin; eye-brows and eye-lids; the hair and its care, etc. Under each heading the approaches to proper care are discussed, formulas are developed, and skillful preparation discussed. Other chapters have such titles as: styptics, depilatories, bath salts, perfumes, toilet waters, shampoos, dentifrices, etc.

The last section of the book deals with technical preparations, such as everyday household needs. Among these are listed: soaps and detergents, bleaching agents, dyes, stain removers, preservatives to be used in canning, air purifiers, insecticides, etc. Also refreshments and alcoholic preparations are discussed as are different goods used by tradespeople and working people, such as brushes, combs, sponges, and other sundries.

It can be justly said that, although there is a very distinct line drawn between the profession of pharmacy and the "Drogist", this book is a valuable addition to the pharmacist's library, since it can serve as a reference book for many useful formulas.

To this reviewer it seems that one or two very important chapters are missing: Photography and photographic equipment, which

is of great importance in the business of a "Drogist", and furthermore, all types of cotton and bandages. Perhaps a later volume will carry information on these two items which used to be available in all "Drogerien."

The book is very well indexed, the illustrations are very clear and very instructive.

E. EHRENSTEIN

Textbook of Physiology, 10th Edition. By William D. Zoethout, Ph. D. and W. W. Tuttle, Ph. D. 710 pages, C. V. Mosbey Co., St. Louis, Mo.

This is an excellent textbook in the field of physiology, written in a clear, concise manner which makes it extremely readable. Among the interesting features of the book are the chapters devoted to isotopes, electrophrenic artificial respiration and suppressor areas of the cerebrum. The chapters on the blood, carbohydrate metabolism, hormones, brain and reproduction are particularly well written.

The material is arranged in the text in logical sequence, and the subjects are correlated with one another. The complete description of the various physiological functions are comprehensive and interesting.

Numerous well-chosen and clearly-drawn diagrams add to the interest. The student, as well as the graduate and the technician, should find this book most valuable.

J. I. FEINMAN

Quinidine in Disorders of the Heart. By Harry Gold, M. D.; 115 pages—1950; New York; Paul B. Hoeber, Inc.; $2.00.

This monograph is written in the manner so characteristic of Dr. Gold's well known and informative lectures and consists of twenty-six chapters. It serves to emphasize the importance of quinidine in the therapy of certain ectopic rhythms of the heart as the result of twenty-five years of the author's personal experience. The author lists the following disorders of cardiac rhythm in which quinidine may be effective: premature contractions or extra systoles (auricular, nodal, and ventricular); paroxysmal auricular tachy-

cardia; nodal tachycardia; auricular flutter; paroxysmal auricular fibrillation; ventricular tachycardia and ventricular fibrillation. Dr. Gold cautions that a large proportion of patients with abnormal rhythm have conditions of no serious consequence. This group requres little if any specific therapy.

The material has been adequately covered in the light of present day knowledge of quinidine and cardiac irregularities. The chapters on indications, toxic actions, tolerance, dosage and the combined use of quinidine and digitalis are especially well done.

The author demonstrates that the dosage of quinidine varies with the patient and the results desired, and, although the conventional 0.2 Gm. (3 grains) three times a day may be effective, as much as 2.0 to 4.0 Gm. (30-60 grains) of quinidine may be necessary to achieve the desired therapeutic results.

Dr. Gold attempts to crystallize the precise therapeutic objectives in the use of quinidine in each particular arrhythmia. He discusses the special action of the drug and its dangers in various situations, illustrated by brief, but pointed histories.

The monograph focuses attention chiefly upon the value of quinidine in the treatment of disorders of cardiac rhythm, but does not neglect its toxicity.

An appended bibliography includes many of the more pertinent articles appearing in the literature since 1906.

This small volume is a worthy addition to the physician's library.

SIDNEY O. KRASNOFF

Fundamental Principles and Processes of Pharmacy. By H. M. Burlage, Ph. D.; J. B. Burt, Ph. D.; C. O. Lee, Ph. D.; and L. W. Rising, Ph. D. Second Edition; 651 pp. incl. index. McGraw-Hill Book Company, Inc., New York, Toronto, London; 1949. Price, $5.00.

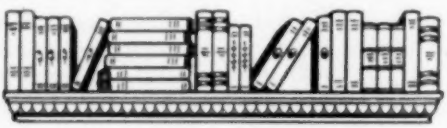
The second edition of this text has brought the contents up to date with the U. S. P. XIII and the N. F. VIII, as well as with some newer concepts of certain principles and processes. Additions have been made to the study questions found at the end of each chapter and also to the collateral reading references. Both of these serve to increase the value of a profitable tool to the pupil who is truly a

student. The collateral reading references also may be of real value as a starting point for the teacher who is seeking to survey the literature relative to a particular subject. Mention should also be made of the addition of a section to the appendix listing various motion picture films available to illustrate the subject matter of the chapters in the text. Teachers recognizing the value of visual aids in teaching should find this listing quite valuable. The authors give a well-placed suggestion that each film should be previewed in order to evaluate the applicability of the contents to the particular course being given. The new type used in this edition deserves comment as to the improved readability of the text.

The elementary principles and processes of Pharmacy are comprehensively and clearly covered in this text. In an attempt to be elementary in approach a few of the more advanced subjects, such as pH, are treated in a manner somewhat less than to be desired. But, the authors no doubt feel that such material will be treated more completely in later courses. One chapter which the reviewer somewhat questions as to the reason for its conclusion in such a text is the chapter on Natural Products Used in Pharmacy. Glycosides, saponins, enzymes and similar subjects are treated in this chapter. In questioning why these subjects were included in the text one must consider the fact that the chemistry and other characteristics of these substances are far from being elementary. However, the authors have attempted to present the information relative to these subjects in a manner as elementary as possible.

The introductory chapters of the text covering ethics, the curriculum, and opportunities in Pharmacy are a valuable introduction to the pharmacist-to-be. Emphasis upon these things are essential in the very beginning as well as throughout the course in order to establish the thinking of the student upon the fact that he is preparing for a profession as distinguished from some other means of livelihood.

K. E. Avis



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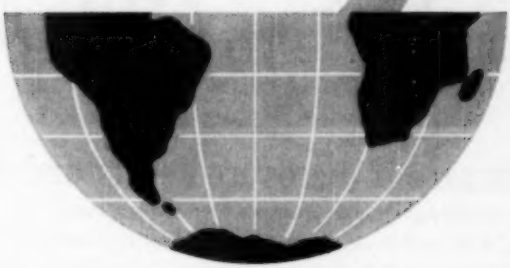

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3. Unusual bleeding or discharge
4. Any change in a wart or mole
5. Persistent indigestion or difficulty in swallowing
6. Persistent hoarseness or cough
7. Any change in normal bowel habits

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